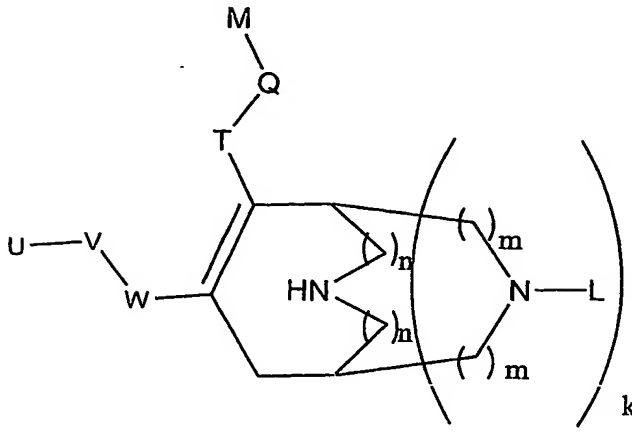
Claims

1. Compounds of the general formula I



General formula I

wherein

W is a six-membered, non benzofused, phenyl or heteroaryl ring, substituted by V in *meta* or *para* position;

V represents –O-CH_2-$CH(OCH_3)$-CH_2-O: -O-CH_2-$CH(CH_3)$-CH_2-O-; -O-CH_2-$CH(CF_3)$-CH_2-O-; -O-CH_2-$C(CH_3)_2$-O-; -O-$C(CH_3)_2$-CH_2-O-; -O-CH_2-$CH(CH_3)$-O-; -O-$CH(CH_3)$-CH_2-O-; -O-CH_2-$C(CH_2CH_2)$-O-; -O-$C(CH_2CH_2)$-CH_2-O-;

U represents aryl; heteroaryl;

T represents -$CONR^1$-; -$(CH_2)_pOCO$-; -$(CH_2)_pN(R^1)CO$-; -$(CH_2)_pN(R^1)SO_2$-; or -COO-;

Q represents lower alkylene; lower alkenylene;

M represents hydrogen; cycloalkyl; aryl; heterocyclyl; heteroaryl;

L represents -R^3; -COR^3; -$COOR^3$; -$CONR^2R^3$; -SO_2R^3; -$SO_2NR^2R^3$;

-$COCH(Aryl)_2$;

R^1 represents hydrogen; lower alkyl; lower alkenyl; lower alkinyl; cycloalkyl; aryl; cycloalkyl - lower alkyl;

R^2 and $R^{2'}$ independently represent hydrogen; lower alkyl; lower alkenyl; cycloalkyl; cycloalkyl - lower alkyl;

R^3 represents hydrogen; lower alkyl; lower alkenyl; cycloalkyl; aryl; heteroaryl; heterocyclyl; cycloalkyl - lower alkyl; aryl - lower alkyl; heteroaryl - lower alkyl; heterocyclyl - lower alkyl; aryloxy - lower alkyl; heteroaryloxy - lower alkyl, whereby these groups may be unsubstituted or mono-, di- or trisubstituted with hydroxy, $-OCOR^2$, $-COOR^2$, lower alkoxy, cyano, $-CONR^2R^{2'}$, -CO-morpholin-4-yl, -CO-((4-loweralkyl)piperazin-1-yl), $-NH(NH)NH_2$, $-NR^4R^{4'}$ or lower alkyl, with the proviso that a carbon atom is attached at the most to one heteroatom in case this carbon atom is sp3-hybridized;

R^4 and $R^{4'}$ independently represents hydrogen; lower alkyl; cycloalkyl; cycloalkyl - lower alkyl; hydroxy - lower alkyl; $-COOR^2$; $-CONH_2$;

k is the integer 0 or 1;

m and n represent the integer 0 or 1, with the proviso that in case m represents the integer 1, n is the integer 0, and in case n represents the integer 1, m is the integer 0; in case k represents the integer 0, n represents the integer 0;

p is the integer 1, 2, 3 or 4;

and optically pure enantiomers, mixtures of enantiomers such as racemates, diastereomers, mixtures of diastereomers, diastereomeric racemates, mixtures of diastereomeric racemates, and the meso-form; as well as pharmaceutically acceptable salts, solvent complexes and morphological forms.

2. Compounds of general formula I according to claim 1 wherein W, V, U, T, Q, L, and M are as defined in general formula I and

k is 1
n is 0
m is 1,

and optically pure enantiomers, mixtures of enantiomers such as racemates, diastereomers, mixtures of diastereomers, diastereomeric racemates, mixtures of diastereomeric racemates, and the meso-form; as well as pharmaceutically acceptable salts, solvent complexes and morphological forms.

3. Compounds of general formula I according to claim 1 wherein W, V, U, T, Q, M, k, m, and n are as defined in general formula I and

L represents $-COR^{3''}$; $-COOR^{3''}$; $-CONR^{2''}R^{3''}$;

$R^{2''}$ and $R^{3''}$ represent independently lower alkyl; lower cycloalkyl - lower alkyl, which lower alkyl and lower cycloalkyl-lower alkyl are undubstituted or mono-substituted with halogen, -CN, -OH, $-OCOCH_3$, $-CONH_2$,-COOH, or $-NH_2$, with the proviso that a carbon atom is attached at the most to one heteroatom in case this carbon atom is sp3-hybridized,

and optically pure enantiomers, mixtures of enantiomers such as racemates, diastereomers, mixtures of diastereomers, diastereomeric racemates, mixtures of diastereomeric racemates, and the meso-form; as well as pharmaceutically acceptable salts, solvent complexes and morphological forms.

4. Compounds of general formula I according to claim 1 wherein W, V, U, L, k, m, and n are as defined in general formula I and

T represents $-CONR^{1}-$;

Q represents methylene;

M represents aryl, heteroaryl;

and optically pure enantiomers, mixtures of enantiomers such as racemates, diastereomers, mixtures of diastereomers, diastereomeric racemates, mixtures of diastereomeric racemates, and the meso-form; as well as pharmaceutically acceptable salts, solvent complexes and morphological forms.

5. Compounds of general formula **I** according to claim 1 wherein W, U, L, T, Q, M, k, m, and n are as defined in general formula **I** and

V represents $-O-CH_2-CH(CH_3)-CH_2-O-$; $-O-CH_2-C(CH_3)_2-CH_2-O-$;

and optically pure enantiomers, mixtures of enantiomers such as racemates, diastereomers, mixtures of diastereomers, diastereomeric racemates, mixtures of diastereomeric racemates, and the meso-form; as well as pharmaceutically acceptable salts, solvent complexes and morphological forms.

6. Compounds of general formula **I** according to claim 1 wherein V, U, T, Q, M, L, k, m, and n are as defined in general formula **I** and

W represents a 1,4-disubstituted phenyl ring,

and optically pure enantiomers, mixtures of enantiomers such as racemates, diastereomers, mixtures of diastereomers, diastereomeric racemates, mixtures of diastereomeric racemates, and the meso-form; as well as pharmaceutically acceptable salts, solvent complexes and morphological forms.

7. Compounds of general formula **I** according to claim 1 wherein W, V, Q, T, M, L, m, and n are as defined in general formula **I** and

U is a mono-, di-, or trisubstituted phenyl or heteroaryl, whereby the substituents are halogen, lower alkyl, lower alkoxy, CF_3

and optically pure enantiomers, mixtures of enantiomers such as racemates, diastereomers, mixtures of diastereomers, diastereomeric racemates, mixtures of diastereomeric racemates, and the meso-form; as well as pharmaceutically acceptable salts, solvent complexes and morphological forms.

8. The compounds according to any one of claims 1 to 7 selected from the group consisting of

(*1R*, *5S*)-7-{4-[(*2S*)-2-methyl-3-(2,3,6-trifluorophenoxy)propoxy]-phenyl}-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid cyclopropyl-(2,3-dichloro-benzyl)amide;

(*1S*, *5R*)-7-{4-[(*2S*)-2-methyl-3-(2,3,6-trifluoro-phenoxy)propoxy]phenyl}-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid cyclopropyl-(2,3-dichloro-benzyl)amide;

a mixture of (*1R*, *5S*)-7-{4-[(*2S*)-2-methyl-3-(2,3,6-trifluorophenoxy)propoxy]-phenyl}-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid cyclopropyl-(2,3-dichlorobenzyl)amide and (*1S*, *5R*)-7-{4-[(*2S*)-2-methyl-3-(2,3,6-trifluoro-phenoxy)propoxy]phenyl}-3,9-diazabicyclo-[3.3.1]non-6-ene-6-carboxylic acid cyclopropyl-(2,3-dichlorobenzyl)amide.

9. Pharmaceutical compositions containing at least one compound of any ones of claims 1 to 8 and usual carrier materials and adjuvants for the treatment or prophylaxis of disorders which are associated with a dysregulation of the renin-angiotensin system (RAS), comprising cardiovascular and renal diseases, hypertension, congestive heart failure, pulmonary hypertension, cardiac insufficiency, renal insufficiency, renal or myocardial ischemia, atherosclerosis, renal failure, erectile dysfunction, glomerulonephritis, renal colic, glaucoma, diabetic complications, complications after vascular or cardiac surgery, restenosis, complications of treatment with immunosuppressive agents after organ transplantation, and other diseases known to be related to the RAS.

10. A method for the treatment or prophylaxis of diseases which are related to the RAS comprising hypertension, congestive heart failure, pulmonary hypertension, cardiac insufficiency, renal insufficiency, renal or myocardial ischemia, atherosclerosis, renal failure, erectile dysfunction, glomerulonephritis, renal colic, glaucoma, diabetic complications, complications after vascular or cardiac surgery, restenosis, complications of treatment with immunosuppressive agents after organ transplantation, and other diseases which are related to the RAS, which method comprises administering a compound according to any one of claims 1 to 8 to a human being or animal.

11. The use of compounds according to any one of claims 1 to 8 for the treatment or prophylaxis of diseases which are associated with the RAS comprising hypertension, congestive heart failure, pulmonary hypertension, cardiac insufficiency, renal insufficiency, renal or myocardial ischemia, atherosclerosis, renal failure, erectile dysfunction, glomerulonephritis, renal colic, glaucoma, diabetic complications, complications after vascular or cardiac surgery, restenosis, complications of treatment with immunosuppressive agents after organ transplantation, and other diseases known to be related to the RAS.

12. The use of one or more compounds of any one of claims 1 to 8 in combination with other pharmacologically active compounds comprising ACE inhibitors, angiotensin II receptor antagonists, endothelin receptor antagonists, vasodilators, calcium antagonists, potassium activators, diuretics, sympatholitics, beta-adrenergic antagonists, alpha-adrenergic antagonists, and neutral endopeptidase inhibitors, for the treatment of disorders as set forth in any one of claims 9 to 11.